REMARKS

Claims 1-11 are pending in the instant application. Claims 12-20 are withdrawn from consideration, as they are drawn to non-elected subject matter. Claims 1-11 stand rejected. None of the claims stand objected to. Applicants herein amend Claim 1, 2 and 6 to clarify the present invention. Applicants have amended the specification to specifically reference prior applications and remove references to a hyperlink or other browser-executable code. These amendments find support in the as-filed specification and claims. No new matter is introduced by the above amendments to the specification or the claims. Applicants respectfully request reconsideration and withdrawal of the rejections for the reasons set forth herein.

REJECTIONS UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 2 and 6 stand rejected under 35 U.S.C. 112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention.

At page 3, of the Office Action, the Examiner contends that in claim 2, identifying manganese as a "substrate" is contrary to art-accepted usage and the recitation of "binding of DXR with a cellular component" is vague and indefinite. Solely to facilitate prosecution, and in no way acquiescing to the Examiner's rejection, the Applicants have amended claim 2 to clarify the scope of the claim. Amended claim 2 no longer recites "binding of DXR with a cellular component" or "use of manganese as a substrate".

In addition, the Applicants have amended Claim 6 (i) and (ii) to replace the recitation of "an polypeptide" with the recitation, "a polypeptide" which is grammatically correct.

The Applicants respectfully submit that Claims 2 and 6, as amended, particularly point out and distinctly claim the instant invention and that the Examiner's rejection under 35 U.S.C. §112, second paragraph should be withdrawn.

REJECTIONS UNDER 35 U.S.C. 35 U.S.C. § 103(a)

Claims 1-11 are rejected under U.S.C. § 103(a) as being allegedly unpatentable over Zeidler *et al.*(1998), Kuzuyama *et al.* (1998), Jomaa *et al.*(1999), Jomaa (WO00/41473) [the English language equivalent, CA 2,360,366 is referenced] and Grolle (2000) in view of Takahashi *et al.* (1998), Croteau *et al.*(US 6, 281, 017) and Sicard *et al.*(2000). Applicants respectfully traverse this rejection.

It is submitted that the combination of Zeidler *et al.,* Kuzuyama *et al.*, Jomaa *et al.,* Jomaa (WO00/41473) [the English language equivalent, CA 2,360,366 is referenced] and Grolle in view of Takahashi *et al.*, Croteau *et al.* and Sicard *et al.* fail to teach or suggest the present invention. Applicants assert that the instant invention is a method for modulating an activity of a DXR reductoisomerase enzyme of *Haemophilus influenzae*, such as modulating the inhibition of DXR by fosmidomycin, which is an activity of DXR. For example, the Applicants are not claiming the small molecule fosmidomycin or inhibiting DXR with fosmidomycin. Therefore, it is submitted that the teachings of the eight references would not lead one of skill in the art to the present invention. None of the references teach or suggest methods of modulating activities of DXR from *Haemophilus influenzae*. In addition, trying to cite references which merely indicate that isolated elements and/or features recited in the claims are known is not sufficient basis for concluding that the combination of claimed elements would have been obvious. See *Ex Parte Hiyamizu*, 10 U.S.P.Q.2d 1393 (Bd.Pat. App. Int. 1988).

However, solely to facilitate prosecution, and in no way acquiescing to the Examiner's rejection, the Applicants amended claims 1 and 2 to clarify the scope of the claim. Claim 1 is amended to provide a negative limitation permitted by MPEP 2173.05(i) Negative Limitations, and Applicants removed elements from claim 2 that reference fosmidomycin, fosfomycin, FR-33289, and FR-900098.

Furthermore, even assuming, *arguendo,* that there is motivation to combine the eight references, which there is not, and that the teachings of the references would lead one of skill in the art to the present invention, Applicants submit that one of skill in the art would not have predicted or expected that DXR from *Haemophilus influenzae* in accordance with the present invention would have advantageously higher minimum inhibitory concentration (herein "MIC") than that of DXR from *E. coli.* For example, in the present application, Applicants have surprisingly shown that the MIC of fosmidomycin increased 16-fold for cells overexpressing *Haemophilus influenzae* DXR in *E. coli* cells (DH5α). (*see* Example 2, Table 3 in the present specification, p. 36), whereas the MIC of fosmidomycin increased only 8-fold for cells overexpressing *E. coli.* DXR in *E. coli* cells (DH5α). (*see* Example 2, Table 2 in the present specification, p. 34). It is submitted that one of skill in the art would not have expected or predictable that the MIC obtained with *Haemophilus influenzae* DXR in accordance with the present invention would be advantageously higher.

The court made it clear that it is improper to reject claims as "obvious to try" where the motivation to combine references arises merely because the subject matter of the claimed

invention is a promising field for experimentation, although the prior art provides only general guidance as to a particular form of the claimed invention or how to achieve it. *In re O'Farrell*, 7 U.S.P.Q.2d 1673, 1681 (Fed. Cir. 1988). Without more specific suggestions in the prior art, there is insufficient motivation to combine the cited references. Furthermore, "focusing on the obviousness of substitutions and differences, instead of the invention as a whole, is a legally improper way to simplify the often difficult determination of obviousness." *Gillette Co. v. S.C. Johnson & Son*, 16 U.S.P.Q.2d 1923, 1927 (Fed. Cir. 1990).

Therefore, obviousness cannot be established by combining the teachings of the references cited to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination." *In re* Geiger, 815 F.2d at 688, 2 U.S.P.Q.2d at 1278. There is no teaching, suggestion or incentive supporting the combination of the eight references because they do not teach methodologies for modulating an activity of *Haemophilus influenzae* DXR. The Examiner's conclusion that a person of ordinary skill in the art would have had a reasonable expectation of success in producing the instant claimed invention given the teachings of Zeidler *et al.*(1998), Kuzuyama *et al.* (1998), Jomaa *et al.*(1999), Jomaa (WO00/41473) [the English language equivalent, CA 2,360,366 is referenced] and Grolle (2000) in view of Takahashi *et al.* (1998), Croteau *et al.*(US 6, 281, 017) and Sicard *et al.*(2000) could only be infered after extensive experimentation and testing. By themselves, the references do not teach exactly how to combine their teachings into the present invention. It is only in hindsight that a way to combine the references can be seen.

In view of the foregoing remarks, the Applicants respectfully request that the Examiner withdraw the rejection of Claims 1-11 under 35 U.S.C. § 103(a).

The Applicants reserve the right to prosecute, in one or more patent applications, the claims to non-elected inventions, the claims as originally filed, and any other claims supported by the specification. The Applicants thank the Examiner for the Office Action and believe this response to be a full and complete response to such Office Action. Accordingly, favorable reconsideration and allowance of the pending and new claims is earnestly solicited.

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If it would expedite prosecution of this application, the Examiner is invited to confer with the Applicants' undersigned agent.

Respectfully submitted,

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